

**REMARKS**

**Amendments to the independent claims**

The independent claims have been amended to limit the list of metals for the formation of eneamide from oxime to the two exemplified metals Iridium (Ir) and Rhodium (Rh) in Examples 1 to 5. These metals were explicitly claimed as preferred metals in pending claim 14, which is therefore cancelled. Accordingly, there is no new matter.

**Claim rejections – 35 USC 103**

The Examiner has maintained rejection of claims 12-21 and 25-26 under 35 USC 103(a) as being unpatentable over Johnson WO99/18065 in view of Tinsley US 3,375,387.

Firstly, the Examiner stated on page 5, item 7 that: “no claim is allowed in absence of a clear delineation of the claims from the prior art and a side by side showing of unexpected results commensurate in scope of the claims”.

It is respectfully submitted that the amendment limiting the list of metals for the formation of eneamide from oxime to the two exemplified metals Iridium (Ir) and Rhodium (Rh) in Examples 1 to 5 renders the claims more commensurate in scope with the unexpected results shown in the Examples.

The Examiner indicated on page 2, last full paragraph, that the catalyst used by Johnson is “a complex of a transition metal M<sup>2+</sup> with a chiral phosphine ligand”.

As emphasized at the Interview on October 14, 2009, Applicants respectfully submit that Johnson teaches the use of a complex of a transition metal M<sup>2+</sup> with a Chiral ligand **exclusively** for the homogeneous ASYMMETRIC HYDROGENATION of the **eneamides** (see Johnson, Page 5, from line 24 to page 6, line 24) which is confirmed by step C of the Johnson’s Examples 1 to 7.

With regard to the formation of eneamides from oximes, Johnson teaches only the critical use of iron (see Johnson, Page 5, lines 9-23) as confirmed by the examples 1 to 7 which use exclusively iron in STEP B. It is indisputable that the relative mole ratio given by Johnson between the iron catalyst and the oxime is 2:1 (see all examples 1 to 7).

In this respect, at the interview it was discussed the unobviousness of the invention as claimed in independent claims 12 and 25, now limited to the two exemplified metals Ir and Rh, with support of unexpected technical results as follows:

a) The main purposes of the preferred embodiments of the invention are to provide a process enabling the large scale preparation of ene-amide derivatives and in good yield, great facility of product isolation, and excellent chemical purity of product and which is reproducible, as it is set forth in the specification paragraphs 1, 7 and 8 of the US published application. These technical results are obtained with the pending claims 12 and 25.

b) Johnson was cited in paragraph 2 of the Applicant's specification with the notation that Johnson's process is unsuitable for large scale production. It was further explained at the interview why Johnson was unsuitable for large scale production. For Example, it appears that Johnson uses iron as a catalyst to transform the oxime into the ene-amide and that it uses twice as much iron as the oxime itself. Accordingly, in large scale production the amount of catalyst would be enormous with regard to the oxime, thereby making the process unsuitable for large scale production and industrialization.

In contrast, in the invention the content of the catalyst is in an amount ranging between 0.001 and 30 mole%, based on the used catalyst. See original claim 4, and pending claims 15 and 25; see also Examples 1 to 5.

c) Applicants therefore respectfully submit that **claim 25**, which is limited to this catalyst/oxime ratio, is unobvious and patentable.

d) In addition it is also believed that claim 12 is also patentable. Indeed, these unexpected results are obtained due to the use of different catalyst selected now from the exemplified metals iridium and rhodium (see amended claims 12 and 25).

Claim 12 provides a scope commensurate with rewarding the inventors for the invention made.

It is indisputable that although Johnson's processes use a similar step of formation of ene-amide from an oxime through catalytic isomerization, an essential technical difference lies in the fact that Johnson performed it solely with iron.

Indeed, an important aspect of the claimed invention is the use of a metal that is not iron, namely, one that is selected from exemplified iridium and rhodium, and that it is sufficient to

provide unexpected results which are implied from the choice of this metal, namely the much lower content of catalyst with regard to the oxime, and/or obtention of better yields.

With regard to the yields, the Examiner said that we had an example at 66% (example 1b) and one at 59.9% (example 1c) and further one example at 57.5% (example 2d) which is close or similar to the percentage of 54% which is obtained by Johnson. See example 5B, page 10, of Johnson.

In this respect, Applicant's Representatives emphasized that one should look not only at the relative ratio between the metal catalyst and the oxime, but also at the temperature of the reaction.

If we look at Johnson's example 5B, the temperature which is used for the reaction is 70°C (page 10, line 23). In contrast, in embodiments of the invention when the yield is relatively low, like in example 2d, first, it is a different product, namely the 6-methoxy-1-indanone, and second, the temperature is only 30°C.

In fact it should be compared to the same synthesis. A direct comparative example is provided for **α-tétralone**, where Example 3 of the application can be compared with Example 5B of Johnson. The invention obtains a yield of 84% with Rh (invention Specification Ex 3a, page 17, line 20,); or 79% with Ir (Ex 3b,), in which the amount of catalyst is only 4% by weight compared to the oxime; whereas Johnson obtains 54% yield with Iron (Fe) (page 10, line 28 of Johnson) in which the amount of iron catalyst (31.2 g) is 69% by weight compared to the oxime (45 g). Thus, Johnson uses almost 20 times more catalyst than the embodiments of Example 3 of the invention. Accordingly, Johnson's method is not extrapolatable to industrial scale.

In view of this, pending claim 12 relates to a patentable invention providing unexpected effects. It is respectfully submitted that it was unobvious for one skilled in the art to replace iron with another catalyst, such as rhodium or iridium set forth in claims 12 and 25, for the critical step of formation of the ene-amide from an oxime of formula II as claimed.

In addition, since Johnson discloses iron as the sole catalyst to prepare the ene-amide from the oxime, Johnson fails to teach or in any way suggest any of the catalysts of the claimed invention, further supporting the unobviousness of the claimed invention over Johnson.

- e) The Examiner is making combination of Johnson with Tinsley US 3,375,287 of 1968.

It should be first observed that this Tinsley patent was published about 30 years prior to the Johnson patent. In view of this, if a combination of Johnson with Tinsley would have been obvious, Johnson would have made it himself.

The fact that the Tinsley reference was as old as 30 years prior to the Johnson invention, already shows the unobviousness of the invention. Moreover, Tinsley teaches that his process is solely applicable to ethylenically unsaturated compounds which are composed solely of carbon and hydrogen, namely a cycloaliphatic nucleus having up to 16 carbon atoms in said nucleus and at least one migratable ethylenic bond. See column 1, lines 26-61 of Tinsley.

This is manifestly not applicable to the oximes to be transformed into ene-amides. Under these conditions, it was nonobvious for one skilled in the art to use the Tinsley technology in the conversion of oximes into ene-amides. This is further corroborated by the fact that Johnson did not use the catalyst previously disclosed in Tinsley, but only iron.

In view of this, absent hindsight made from knowledge of the invention, it is apparent that the invention as claimed is nonobvious for one skilled in the art to which the invention pertains.

In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Please charge any additional fees or credit any overpayment to Deposit Account No. 13-2725.

Respectfully submitted,

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